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Occupational Cancers with Special Reference to Laboratory Personnel

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Occupational Cancers with Special Reference to Occupational Cancer Hazards to Laboratory Personnel

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An increasing amount of epidemiologic, pathologic, clinical, and experimental evidence acquired during recent decades supports the view that many human cancers are directly or indirectly related to contacts with certain specific environmental, physical, and chemical agents to which the population becomes exposed for occupational, medicinal, dietary, or other environmental reasons (table 1).

Among the numerous and diverse claims advanced concerning the causation of human cancers, these data provide indeed the only factual and well-established information in such matters. The data on hand strongly indicate that the same agents that cause occupational cancers most probably are also responsible for similar cancers occurring among members of the general population because of the dissemination of the occupational carcinogens into the general human environment as parts of industrial pollutants of the air, water, and soil, and as constituents or impurities in consumer goods. The majority of cancers of the skin, for instance, can be traced to exposures to recognized environmental carcinogens, such as sunlight, ionizing radiations, coal tar and pitch, lubricating and cutting oils derived from petroleum, and arsenicals.

Table 1: Occupational Carcinogens, Their Route of Exposure and Their Target Organs

General Type	Specific Type	Route of Exposure	Target Organs
Chemical Carcinogens Organic chemicals: Aromatic Polycyclic Heterocyclic	Benzol Beta-naphthylamine Benzidine 4-Aminodiphenyl Auramine	Cutaneous Respiratory Respiratory Cutaneous Alimentary	Blood-forming organs (leukemia, lymphosarcoma) Urogenous organs (bladder, ureter, kidney) Lung? Intestine?
	Coal tar, pitch, asphalt, tar oil, creosote oil, anthracene oil, lamp black, lignite tar, and paraffin oil	Cutaneous Respiratory	Skin Lung
	Synthetic hydrogenated coal oil and tar (bergius)	Cutaneous	Skin
	Shale oil and paraffin oil	Cutaneous Respiratory	Skin Larynx
	Petroleum fuel oil, diesel oil, lubricating oil and grease, cutting oil, carbon black, asphalt, tar, coke, crude paraffin oil	Cutaneous Respiratory	Skin Lung
Aliphatic	Isopropyl oil	Respiratory	Nasal sinus, larynx, lung
Chemical carcinogens	Mustard gas	Respiratory	Lung, larynx?
Inorganic chemicals	Arsenic	Cutaneous, ingestive	Skin, nasal sinus, lung, liver
	Nickel	Respiratory	Nasal cavity, nasal sinus, lung
	Chromium	Respiratory	Lung, nasal cavity, nasal sinus
	Asbestos	Respiratory	Lung, pleura
Physical carcinogens	Ultraviolet radiation	Cutaneous	Skin
Ionizing radiation	X-Radiation	Cutaneous Transcutaneous	Skin Connective tissue, bone, blood-forming organs
	Radioactive radiation (alpha, beta, and gamma radiation)	Cutaneous Transcutaneous Respiratory Ingestive parental	Skin Connective tissue, blood-forming organs Nasal sinus Lung, bone, liver
Parasite carcinogens	Schistosoma, haematobium	Cutaneous	Bladder

The development of many cancers of the lung seem to be related to exposures to known environmental carcinogens, such as polycyclic hydrocarbons contained in coal tar fumes, coal pitch dust, cutting oil mists, exhaust fumes from automobiles, dusts and fumes containing arsenicals, chromates, nickel compounds, asbestos, and radioactive chemicals. Similar relations to environmental carcinogens prevail for cancers of the bladder, bones, blood forming organs, alimentary tract, and liver.

There exists a considerable number of additional chemicals that must be suspected of exerting, at least in part, similar carcinogenic effects on man upon proper contact. However, at present the evidence incriminating these compounds, which mostly form newly added constituents of our modern industrial economy with which large parts of the population often have frequent and intimate contact, is not sufficiently adequate or too fragmentary for definitely incriminating them at this time in the production of cancers in man (table 2). They must be considered, however, as potential human carcinogens until their innocuousness to man can conclusively be established.

Since the most readily demonstrable and usually most intense exposures to the various occupational and industry-related carcinogens takes place in general among members of certain industrial worker groups, the majority of known cases of cancers caused by these environmental carcinogenic agents was observed in such population groups. However, the occurrence of occupational cancers has not remained restricted to specific worker groups engaged in the production, processing, handling, and using these industrial carcinogens. In fact, a few occupational cancers have been observed preferentially among members of certain professions, such as radiologists. Considering the fact that an effective therapeutic control of many cancers is still to be obtained, it is important to note here that the development of the great majority of occupational cancers can successfully be prevented by available precautionary measures

Table 2: Potential Environmental Human Carcinogens

Agent	Site of Tumor	Type of Exposure	Species	Types of Human Contact
Estrogens, natural, synthetic	Breast Lymph nodes Uterus Hypophysis	Parenteral Cutaneous Oral	Mouse Rat Rabbit Guinea pig	Manufacture Dietary additive Cosmetic ingredient
Carbon tetrachloride	Liver	Oral	Mouse	Industrial solvent, degreasing agent, dry cleaning agent, manufacture production of Freon, grain fumigant, extractive of oils
Chloroform	Liver	Oral Parenteral	Mouse	Manufacture Anesthetic Solvent and extractive of oils, resins, rubber, waxes, iodine, alkaloids Ingredient of lacquer, floor polish, cleaning fluid Production of artificial silk, plastics
DDT	Liver	Oral	Rat Dog	Manufacture Insecticide Food contaminant
Aramite **Tannic acid**	Liver Liver	Oral Parenteral	Rat, dog Rat	Miticide Ingredient of foodstuffs (fruits, wine, coffee, and tea) Medicinal agent Tanning agent
Polyoxymethylene (8) stearate	Bladder	Oral	Rat	Emulsifier in bread
Thiourea and derivatives **Thioacetamide** **Dulcin**	Liver Thyroid Liver, bladder	Oral	Rat	Citrus fruit preservative Medicinal agent Sweetening agent
Diethylene glycol	Bladder	Oral	Rat	Antifreeze Intermediate in explosive manufacture Softener of lacquer, inks, wood stains, glue, textiles Humectant, tobacco
8-Hydroxyquinoline	Uterus	Vaginal	Mouse, Rat	Contraceptive, disinfectant
Methylated-naphthalenes	Skin	Cutaneous	Mouse	Vehicle of insecticides
Bergius coal oils, tars	Skin Subcutaneous tissue	Cutaneous Parenteral	Mouse	Manufacture Fuel Lubricants Plastic production Petrochemical
Beta-propiolactone	Skin	Cutaneous	Rat, Mouse	Viricide (vaccine, plasma, room and air disinfectant)
Fischer-Tropsch coal oils, tars, waxes, greases	Liver	Cutaneous Parenteral	Mouse	Manufacture Fuel Lubricants Petrochemical
Aminotriazole **Light green, SF** **Brilliant Blue, FCF** **Butter Yellow**	Thyroid Subcutaneous tissue Liver	Oral Parenteral Oral	Rat Rat Mouse, Rat	Herbicide Textile dyes Food and cosmetic dyes Food dye (Orient) Gasoline and flare dye
Cellophane **Polyethylene** **Polyamide** **Bakelite**	Subcutaneous	Parenteral	Rat	Film, fiber, plastic-industrial manufacture and uses Wrapping material Medicinal agent
Iron-Dextran	Subcutaneous tissue	Subcutaneous	Rat, Mouse	Anti-anemic drug
Beryllium	Bone	Parenteral Respiratory	Rabbit Rat	Metal alloy, X-ray tube, phosphor manufacture Refractory vessels Atomic energy production
Selenium	Liver Thyroid	Oral	Rat	Soil contaminant Coloring matter of glass, ceramics, paint, rubber Metal alloys Rubber accelerator Photoelectric apparatus Decolorizer Fireproofing agent Medicinal agent

The most essential requirement preliminary to accomplishing a preventive control of occupational cancers is the proper awareness of the exposed individuals, of the existence, types, and sources of occupational cancer hazards. It is the particular purpose of this presentation to alert technologists employed in medical laboratories to cancer hazards that may be associated to agents handled, and activities pursued in such establishments.

1. Benzene or Benzol

Benzol or benzene is a leukemogenic agent that has caused leukemia among rubber cement workers employed in rubber factories and canned food plants, painters, rotogravure printers, and chemical workers. Exposed persons may exhibit first aplastic hematic effects before hyperplastic and leukemoid manifestations appear. Skin contact with benzene or inhalation of benzene vapors sustained during laboratory operations requiring the use of benzene as a vehicle or diluent; as a solvent in the extraction of oils, fats, and lipoids; or as an eluent of chromatographic studies might prove dangerous if occurring frequently. Such laboratory procedures, therefore, should best be carried out in a hood or with adequate exhaust ventilation. Laboratory workers routinely doing such work and having such contacts should be kept under periodic medical surveillance, including blood examination, for evidence of injury to the blood-forming tissues. Evidence of hematic damage is an indication of the inadequacy of the precautionary measures used. Injured individuals require often a prolonged period of medical care and absence from work for complete recovery. It is important from a clinical as well as medico-legal viewpoint that the leukemic phase of chronic benzene injury may become manifest several months after apparent recovery from a primary degenerative phase. Since benzene is retained and stored in the fat tissue of the bone marrow, it may nevertheless be possible at such a time to demonstrate benzene in this tissue by chemical analysis. Such a test has been positive some months after cessation of exposure to benzene. The occupational origin of a leukemia can thereby be established.

2. Aromatic Amines

Several aromatic amines, namely, beta-naphthylamine, benzidine, and 4-aminodiphenyl, have caused cancers of the bladder following a cutaneous and respiratory exposure among producers of these dye and rubber antioxidant intermediates, and among their users in the manufacture of azo-dyes and rubber antioxidants as well as among rubber workers. These chemicals are readily absorbed through the skin and are highly potent human carcinogens, accounting for over 2,000 cases of bladder cancer among German, Swiss, English, Italian, American, Russian, and Japanese dye workers.

The total number of cancers caused by occupational and environmental agents (dietary, cosmetic) is doubtlessly considerably higher than this number because many of these cases were either not properly recognized concerning their specific environmental etiology or were not reported. Since beta-naphthylamine has recently been demonstrated as an impurity in two formerly certified food, drug, and cosmetic dyes, namely, yellow AB and yellow OB, and since these dyes were until recently certified for external cosmetic use, the number of persons who became exposed for many years to beta-naphthylamine through the consumption of margarine, butter, cheese, and cookies colored with these dyes is indeed very high. It is, on the other hand, unknown whether any bladder cancers have resulted from such prolonged exposures.

Employees in medical laboratories may have contact with beta-naphthylamine, if this chemical is produced and/or used on tissue sections for the histochemical demonstration of certain proteinases. If, in such procedures, beta-naphthylamine containing solutions and containers are not handled with extreme caution so as to avoid undue contact, particularly by their spillage on bench tops and floors, not only technologists but also cleaning personnel may sustain an effective exposure to beta-naphthylamine. Because beta-naphthylamine does not elicit any acute or chronic toxic symptoms, such contacts may not attract any attention until after several years. Suddenly and without warning symptoms, the appearance of blood in the urine and other urinary disturbances signify the presence of a bladder cancer. These cancers, like any other occupational cancer, may develop many years after cessation of exposure to the carcinogenic agent.

The extreme degree of cancer hazard created by an occupational contact with beta-naphthylamine, which is measured in terms of micrograms when sustained over some months or years, is evident from the fact that the dye industries in Germany, England, Switzerland, and in part also in the United States have discontinued for a number of years the production of beta-naphthylamine because of its extreme and technologically uncontrollable occupational cancer hazard. The demonstration of 2-amino-1-naphthol sulfate or glucuronate in the urine may serve at times as a diagnostic sign of an exposure to beta-naphthylamine.

Benzidine is of slightly lesser carcinogenic potency than beta-naphthylamine. Benzidine has been used for many years for the demonstration of occult blood in urine, feces, and gastric content. From more recent experiences made in industry it appears likely that benzidine does not only cause cancer of the bladder but also of other organs, such as the intestine and lung.

Although the occurrence of bladder cancer among technologists of medical laboratories from contact with these aromatic amines has as yet not been reported, such sequelae have been recorded among laboratory workers in the chemical industry handling benzidine and beta-naphthylamine, among cleaning personnel and among laundresses washing work clothes contaminated with these aromatic amines. These observations indicate that distinct precautions and extreme cleanliness are necessary whenever carcinogenic aromatic amines are handled, processed, or used in a medical laboratory.

Adequate protection demands that these chemicals be used only in a hood for avoiding contact with dust and vapors, and the contamination of rooms from spilled solutions. Since it has been alleged in the past years that males are mainly or only susceptible to the carcinogenic action of these aromatic amines, it may be mentioned that bladder cancers have experimentally been produced with beta-naphthylamine in female dogs and that recent reports from USSR and Italy noted their occurrence among female dye workers.

3. Coal Tar, Pitch, Petroleum Oils, Paraffin, Asphalts, and Carbon Blacks

Medical technologists, as a rule, have little opportunity for a frequent and intimate contact with the carcinogenic products of the distillation and combustion of coal, petroleum, and related carbonaceous matter. It may be mentioned, however, that crude paraffin oils as well as insufficiently refined paraffin waxes are carcinogenic to the skin and lung. Histologic technologists, therefore, may be advised to avoid a frequent inhalation of fumes from heated paraffin waxes and should not adopt the habit of chewing paraffin plugs. Similar precautions should be applied to the use of mineral oil baths for chemical procedures. Burns caused by hot mineral oil or wax should thoroughly be cleaned to prevent retention of any oily or waxy matter in the injured tissue that might give rise to a subsequent development of a cancer.

4. Arsenic, Chromium, Nickel, Asbestos

It is not likely that the working conditions and practices in medical laboratories are associated with effective exposures to the various carcinogenic minerals, such as arsenic, asbestos, chromium, and nickel. These have resulted in occupational cancer hazards leading to the development of cancers of the respiratory organs, i.e., lung, larynx, nasal cavity and nasal sinuses, and, for arsenicals also, of the skin and liver. Effective exposures may occur, however, for those medical technologists who are attached to medical departments located on the premises and thus in the dust and fume zone, of chromate producing plants, nickel refineries, copper smelters using arsenic-containing ores, and asbestos mills and textile plants. The observations of a perforated nasal septum in a nurse employed in an American chromate plant attests to the actual existence of such exposure conditions for medical personnel working in industrial medical establishments located within the immediate neighborhood of such plants.

5. Ultraviolet Radiation

Cancers of the exposed skin appearing in man, mice, and rats after an excessive and prolonged exposure to solar radiation, and ultraviolet radiation from mercury or carbon arcs and following the development of a precancerous actinic dermatitis, furnish definite proof of the carcinogenic action of ultraviolet rays. The carcinogenic action of this actinic energy upon the human skin accounts for the high frequency of cancers of the exposed skin among the inhabitants of our Midwestern, Southwestern, Western, and Southern states, including Florida, Southern California, and Hawaii. Technologists working in heliotherapy and ultraviolet therapy departments when sustaining excessive exposures to ultraviolet radiation, unless they observe the proper protective precautions, may develop occupational cancers of the skin.

Most susceptible to the carcinogenic action of ultraviolet radiation is the skin of fair-complexioned individuals who do not tan upon exposure but burn. Brunette whites show a somewhat higher resistance. Chinese, Japanese, Filipinos, and members of related races are even more resistant than whites, while deeply pigmented Negroes appear to be entirely refractory to the development of solar cancer of the skin. Such environmental and occupational cancers are often multifocal and appear in a skin showing signs of a chronic solar dermatitis, also known as farmer’s skin and sailor’s skin, since such occupational conditions occur not infrequently among members of these population groups.

Individuals who display a special constitutional liability to solar cancers and become frequently exposed for occupational or other reasons to ultraviolet radiation, therefore, should wear adequate clothing and hats with wide brims, and might additionally apply protective creams to avoid cancerous sequelae.

6. Ionizing Radiations

Medical technologists have been among the early victims of X-ray cancers of the skin following the introduction of roentgen-rays into medical practice in 1895. It was only a few years later that this sad experience was repeated in medical personnel handling radioactive substances for therapeutic purposes as well as in patients who had received excessive amounts of X-rays. Such occurrences were rather frequent among the pioneers of radiology, because the cancer hazard from exposure to ionizing radiation was not known or sufficiently appreciated during the early days. The actual number of victims of occupational radiation cancers is unknown. For several decades, cancer hazards from ionizing radiation for laboratory personnel remained restricted to radiations generated by X-ray tubes and given off by radium, radon, and mesothorium employed in diagnostic and therapeutic medical practice.

It was only in more recent years that the growing use of electron microscopes, X-ray diffraction apparatus, and television projection equipment added for certain types of laboratory personnel a few new sources of radiation hazards resulting from the production of X-rays by electron guns. A considerable expansion and diversification of radiation hazards to medical technologists have resulted from the increasing use of radioisotopes for diagnostic and therapeutic use into medical practice during the last fifteen years. Unless such materials are handled with distinct caution, cancer hazards from contact with radioisotopes may ensue not only for the regular technologists in charge of such materials but also for other members of the laboratory staff, such as histological assistants, cleaning personnel, and attendants of autopsy rooms.

The type of target organ of any cancerous response to such radioactive materials depends on the kind of radioisotope as well as on the route or contact or introduction into the body. Cancers of the skin may be caused by external exposures to X-radiation and emitters of beta and gamma rays. The inhalation of radioactive gases and dust may elicit cancers of the lungs and nasal sinuses. Penetrating radiation by X-rays or deposition of radioactive substances after inhalation or ingestion in the bone may produce cancers of the bone and leukemia (radiostrontium-90, radiophosphorus). Storage of radioactive matter such as thorotrast, in organs of the reticuloendothelial system, such as the liver and the spleen, may be followed by the development of hemangio-endotheliomas of these organs.

The appearance of cancers of the skin is usually preceded by the development of a chronic radiodermatitis, that of cancers of the bone by a chronic periostitis, and that of leukemia by aplastic (leukopenia, anemia) and hyperplastic (leucocytosis, monocytosis, leukemoid reactions) responses of the blood-forming tissues. The latent period may range from two to thirty years, and therefore may be much longer than the exposure time, which, with powerful exposures, may be very short, i.e., minutes. Radiation burns of the skin produced by a single exposure to X-rays may give rise to cancers of the skin appearing many years later.

In addition to these exposures to recognized occupational carcinogens, medical technologists may have contact with a number of potential human carcinogens, i.e., chemicals for which the available incriminating evidence concerning their carcinogenic properties for man is controversial, or for which only positive observations on experimental animals exist. Carcinogens of this type are natural and synthetic estrogens, carbon tetrachloride, chloroform, diethylene glycol, thiourea derivatives, and beta-propiolactone.

In summary it may be stated that medical technologists may become effectively exposed to a number of recognized or suspected human carcinogens during the performance of their regular work. Cancer hazards associated with such exposures may effectively be prevented by the observation of suitable precautionary measures. Technologists, therefore, should be aware of these hazards and should familiarize themselves with the proper control measures for preventing the development of such avoidable occupational cancers.

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